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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/994,937	11/28/2001	David M. Anderson	05900002AA	7327

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EXAMINER	
FISHER, ABIGAIL L	
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	09/994,937	ANDERSON, DAVID M.	
	Examiner	Art Unit	
	ABIGAIL FISHER	1616	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *15 September 2010*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *66-68 and 70-107* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *66-68 and 70-107* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on September 15 2010 has been entered.

Receipt of Amendments/Remarks filed and Declaration under 37 CFR 1.132 on September 15 2010 is acknowledged. Claims 1-65, 69 and 108-111 were/stand cancelled. Claims 66-68, 72 and 98-103 were amended. Claims **66-68 and 70-107** are pending.

Rejections and/or objections not reiterated from previous office actions are hereby withdrawn. The following rejections and/or objections are either reiterated or newly applied. They constitute the complete set presently being applied to the instant application.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claim 72, 79 and 85 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claims 72, 79 and 85 introduce new matter as the claims recite the limitation: "pharmaceutical active is greater than 5% soluble in said essential oil ". There is no support in the specification for this limitation. The limitation of the pharmaceutical agent being greater than 5% soluble in the essential oil was not described in the specification as filed, and person skilled in the art would not recognize in the applicant's disclosure a description of the invention as presently claimed. The specification discloses that paclitaxel is soluble at specific percentages in specific oils. While these percentages are greater than 5%, this does not support the limitation for all pharmaceutical actives being greater than 5% soluble in the essential oil nor does it support paclitaxel being soluble in all values above 5% in the essential oils. Support is only for a specific drug (paclitaxel) as specific concentrations. Therefore, it is the Examiner's position that the disclosure does not reasonably convey that the inventor had possession of the subject matter of the amendment at the time of filing of the instant application.

Response to Arguments

Applicants argue that the concept of the pharmaceutical agent being greater than 5% soluble in an essential oil is taught when the totality of paragraphs 235 and 236 and the table there between are considered.

Applicants' arguments filed September 15 2010 have been fully considered but they are not persuasive.

While the concept of the pharmaceutical active being more soluble when the essential oil is present than when the essential oil is not present is taught. The claimed degree of solubility is not taught for all pharmaceutical agents. The greater than 5% for paclitaxel is based on its interaction with a specific essential oil. This does not provide support for the claimed degree of solubility for all pharmaceutical agents.

Claims 68, 83-89, 92, 94, 97 and 101-103 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claims 68 and 101-103 introduce new matter as the claims recite the limitation: "excluding anisole". There is no support in the specification for this limitation. The limitation of: "excluding anisole" was not described in the specification as filed, and person skilled in the art would not recognize in the applicant's disclosure a description

of the invention as presently claimed. The specification discloses essential oils and anise oil but does not describe the instantly claimed limitation. In order to specifically exclude an element the specification must either positively or negatively recite the excluded element. There is no guidance in the specification to select anisole (either positively or negatively) and from MPEP 2163.06: "Applicant should therefore specifically point out the support for any amendments made to the disclosure." Applicant has not directed the Examiner to the support in the specification for the amendments. Therefore, it is the Examiner's position that the disclosure does not reasonably convey that the inventor had possession of the subject matter of the amendment at the time of filing of the instant application.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 66, 70-71, 73-74, 90, 95, 98, 100, 104 and 106 are rejected under 35 U.S.C. 102(b) as being anticipated by Anderson (WO 9912640, cited in the Office action mailed on 6/16/09) as evidenced by Evans (US Patent No. 5026548, cited in the Office action mailed on 3/16/10), Burdock (Food and Color Additives, 1997, cited in the Office action mailed on 3/16/10) and Muldoon et al. (Systematic Organic Chemistry, 1957, cited in the Office action mailed on 3/16/10).

Anderson et al. exemplify a cubic phase liquid crystal formulation comprising soy lecithin (epikuron 200) in 0.345 g, anisole in 0.357 g, water and Paclitaxel (example 37).

As evidenced by Evans et al., Epikuron 200 is fractionated soya lecithin containing 92% phosphatidylcholine (column 12, lines 13-14).

As evidenced by Muldoon et al., anisole is found in anise oil (page 567). As evidenced by Burdock, anisole can be chemically synthesized as well as found in natural sources such as olive, artichoke, vanilla, etc. (page 178-179, anisole section).

Therefore, Anderson exemplify a composition comprising a cubic phase, water, phospholipid, component of essential oil and a pharmaceutical active.

Regarding the claimed ratio of phospholipid to essential oils or component thereof. The ratio exemplified is 0.97 to 1.

Response to Arguments/Declaration under Rule 132

The declaration under 37 CFR 1.132 filed September 15 2010 is insufficient to overcome the rejection of claims 66-68 and 70-107 based upon Anderson (WO 9912640) as set forth in the last Office action because: firstly the figures shown in point 4 are incomprehensible. The figures are so dark that one can not make heads or tails of what is shown in the figures. Secondly, numerous points given by applicant are his opinion rather than fact. Opinion on the ultimate legal conclusion at issue is not entitled to any weight, although the underlying basis for the opinion may be given some weight. While applicant may not agree that anisole is not an essential oil, since neither the specification nor claims provide a limiting definition of essential oil the broadest

reasonable interpretation will be utilized. Based on the evidenced presented by the examiner above (specifically Muldoon et la. And Burdock) anisole broadly reads on a component of an essential oil. Regarding the issue of solubilization, while Anderson does speak of the compositions being metastable, Anderson explicitly states in the examples that if the concentration of paclitaxel in this system were lowered then the solubilization of Paclitaxel becomes a truly stable solubilization (thermodynamic equilibrium) so that precipitation is prevented altogether (Example 36). The above rejected claims require no degree of solubilization. Therefore, the exemplified compositions of read on the instantly claimed composition. While Anderson may describe coated particles and applicant argues this is why they are not concerned with precipitation. However, the presence of a coating is not excluded by the currently claims. Therefore, Since Anderson exemplifies a composition comprising the same claimed components the rejection is maintained.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Applicant Claims
2. Determining the scope and contents of the prior art.
3. Ascertaining the differences between the prior art and the claims at issue, and resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 67-68, 72, 75-89, 91, 93-94, 96-97, 99 and 101-103 are rejected under 35 U.S.C. 103(a) as being unpatentable over Anderson as evidenced by Evans, Burdock and Muldoon et al.

Applicant Claims

The instant application claims a composition comprising A) a reversed cubic liquid phase comprising water; a phospholipid; tocopherol, and B) a pharmaceutical active solubilized in said structured fluid.

The instant application claims a composition comprising A) a reversed cubic liquid phase comprising water; a phospholipid; an essential oil or component thereof or tocopherol, and B) a pharmaceutical active solubilized in said structured fluid.

Specific essential oils claimed include anise oil and peppermint.

Specific drug claimed include daunorubicin.

Determination of the Scope and Content of the Prior Art (MPEP §2141.01)

Anderson is directed to coated particles that comprise an internal core comprising a matrix and an exterior coating. The nanostructured liquid crystalline phase material may be formed form a polar solvent, a surfactant and an amphiphile or hydrophobe (page 34, lines 7-11). Example 36 comprises Paclitaxel, eugenol, soy lecithin (epikuron 200) and glycerol. Example 37 comprises soy lecithin (epikuron 200), anisole, water and Paclitaxel. The preferred amphiphile and hydrophobe components (third component) include anise oil, clove oil, peppermint oil; eucalyptus oil; eugenol; vitamin E, etc. (pages 37-38 lines 29-32 and 1-4). Examples of active agents when can be solubilized besides paclitaxel include daunorubicin (page 45, line 22).

Ascertainment of the Difference Between Scope the Prior Art and the Claims (MPEP §2141.012)

While Anderson teach preferred third components include anise oil, peppermint oil and vitamin E, Anderson does not exemplify formulations with these components.

While Anderson teach that the drug delivered can be daunorubicin, Anderson do not exemplify formulations with daunorubicin.

Finding of Prima Facie Obviousness Rational and Motivation (MPEP §2142-2143)

It would have been obvious to one of ordinary skill in the art at the time of the instant invention formulate a composition wherein the paclitaxel is dissolved in water, phospholipid and tocopherol or an essential oil such as anise oil or peppermint oil. One of ordinary skill in the art would have been motivated to utilize these three components

for solubilizing paclitaxel as Anderson teaches that the nanostructured liquid crystalline phase material may be formed from a polar solvent, a surfactant and an amphiphile or hydrophobe and exemplify a formulation comprising water (polar solvent), soy lecithin (phospholipid, surfactant) and anisole (amphiphile or hydrophobe). Therefore, it would have been obvious to one of ordinary skill in the art to substitute the exemplified amphiphile or hydrophobe with other preferred hydrophobes such as tocopherol or essential oils like anise oil or peppermint oil. It would have been obvious to one of ordinary skill in the art to try any of the specifically taught preferred third components as a person with ordinary skill has good reason to pursue known options within his or her technical grasp. **Note: MPEP 2141 [R-6]** *KSR International CO. v. Teleflex Inc.* 82 USPQ 2d 1385 (Supreme Court 2007).

It would have been obvious to one of ordinary skill in the art at the time of the instant invention to substitute the exemplified drug Paclitaxel for other specifically taught drugs such as daunorubicin. It would have been obvious to one ordinary skill in the art to vary the drug in the formulation depending on the disease or condition to be treated. Therefore, one of ordinary skill in the art would have been motivated to utilize daunorubicin in place of the exemplified paclitaxel when desiring to deliver an antibiotic.

Regarding the claimed ratio of phospholipid to tocopherol, the exemplified ratio of phospholipid to third component is 0.97 to 1. Since tocopherol is an alternative third component it would have been obvious to utilize it in the same amount as the exemplified third component.

Absent any evidence to the contrary, and based upon the teachings of the prior art, there would have been a reasonable expectation of success in practicing the instantly claimed invention. Therefore, the invention as a whole would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made.

Response to Arguments/Declaration under Rule 132

Applicant's arguments filed December 15 2009 have been fully considered but they are not persuasive.

The third component would just be the only component that is variable compared to the instant composition. Numerous essential oils are clearly taught. Therefore, the examiner maintains it would have been obvious to substitute the exemplified anisole with other essential oils such as anise oil and peppermint oil. Applicants have not demonstrated the unobviousness of the specifically claimed components compared to the markush taught by Anderson. Since Anderson teaches that a true solution can be achieved by lowering the amount of paclitaxel, a solution is contemplated and therefore the compositions read on the instantly claimed compositions. Regarding claims 72, 79 and 85 which recite specific degrees of solubilization, Anderson clearly makes the use of anisole and peppermint oil obvious. Since these are the same essential oils claimed and paclitaxel is a pharmaceutical agent which reads on the instantly claimed pharmaceutical agent, the examiner does not understand how the solubilities would not be the same. Note MPEP 2112.02 (1I): "Products of identical chemical composition can not have mutually exclusive properties." A chemical composition and its properties are

inseparable. Therefore, if the prior art teaches the identical chemical structure, the properties applicant discloses and/or claims are necessarily present. In re Spada, 911 F.2d 705,709, 15 USPQ2d 1655, 1658 (Fed. Cir. 1990). Therefore a composition comprising peppermint oil and paclitaxel would have the claimed solubility.

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to ABIGAIL FISHER whose telephone number is (571)270-3502. The examiner can normally be reached on M-Th 9am-6pm EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Johann Richter can be reached on 571-272-0646. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Abigail Fisher
Examiner
Art Unit 1616

AF

/Mina Haghighatian/
Primary Examiner, Art Unit 1616